Practitioner's Docket No. MPI00-343P1RM

IN THE SPECIFICATION:

At page 1, in the Title, please replace the Title with the following corrected text:

ACTR-1~~-ATCR-1~~, A NOVEL HUMAN ACYLTRANSFERASE AND USES THEREOF

At page 5, lines 8-20, please replace the paragraphs with the following corrected paragraphs:

Figure 7 is a graph depicting the relative expression of ACTR-1~~-ATCR-1~~ in various human tissues as determined by a TaqMan® Quantitative Polymerase Chain Reaction analysis.

Figure 8 is a graph depicting the relative expression of ACTR-1~~-ATCR-1~~ in various human tissues as determined by a TaqMan® Quantitative Polymerase Chain Reaction analysis.

Figure 9 is a graph depicting the relative expression of ACTR-1~~-ATCR-1~~ various liver, heart and adipose tissues as determined by a TaqMan® Quantitative Polymerase Chain Reaction analysis.

Figures 10A is a graph depicting cholestyramine regulation of ACTR-1~~-ATCR-1~~ expression in a marmoset animal model. *Figure 10B* is a graph depicting the results of a slot blot validation of cholestyramine regulation of ACTR-1~~-ATCR-1~~ in the marmoset animal model.

At page 5, line 23 through page 26, line 3, please replace the paragraph with the following corrected paragraph:

The present invention is based, at least in part, on the discovery of novel acyltransferase family members, referred to herein as "Acyltransferase-1" or "ACTR-1" nucleic acid and protein molecules. Based on their homology to mouse and rat Glycerol-3-phosphate acyltransferases (see *e.g.*, Figure 5) the ACTR-1 proteins of the present invention can be referred to interchangeably throughout as human GPAT protein and/or nucleic acid molecules. These molecules are novel members of a family of enzymes which are capable of catalyzing the transfer of an acyl group to biological molecules (*e.g.*, lipids, polypeptides) and, thus, play a role in or function in a variety of metabolic and cellular processes, *e.g.*, lipid and protein acylation, intra- or inter-cellular communication (*e.g.*, signal transduction), gene expression, hormonal responses, immune responses, energy homeostasis (*e.g.*, the metabolism of biochemical molecules necessary for energy production or storage), and/or cellular proliferation, growth, differentiation, homeostasis, or migration. In particular, the ACTR-1~~-ATCR-1~~ molecules of the invention are capable of catalyzing the transfer of a fatty acyl CoA to the sn-1 position of glycerol-3-phosphate, *i.e.*, during the synthesis of triglyceride. Thus, the ACTR-1 molecules of the present invention provide novel diagnostic targets and therapeutic agents to control ACTR-1-associated or acyltransferase-associated disorders and/or triglyceride-associated disorders, as defined herein.

At page 11, lines 1-35, please replace the paragraphs with the following:

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The present invention provides methods for identifying the presence of an ACTR-1 ~~ATCR-1~~ nucleic acid or polypeptide molecule associated with a cardiovascular disorder or a triglyceride metabolism disorder. In addition, the invention provides methods for identifying a subject at risk for a cardiovascular disorder, or a triglyceride metabolism disorder, by detecting the presence of an ACTR-1 ~~ATCR-1~~ nucleic acid or polypeptide molecule.

The invention also provides a method for identifying a compound capable of treating a cardiovascular disorder or triglyceride metabolism disorder, characterized by aberrant ACTR-1 ~~ATCR-1~~ nucleic acid expression or ACTR-1 ~~ATCR-1~~ protein activity by assaying the ability of the compound to modulate the expression of an ACTR-1 ~~ATCR-1~~ nucleic acid or the activity of an ACTR-1 ~~ATCR-1~~ protein. Furthermore, the invention provides a method for treating a subject having a cardiovascular disorder or a triglyceride metabolism disorder characterized by aberrant ACTR-1 ~~ATCR-1~~ protein activity or aberrant ACTR-1 ~~ATCR-1~~ nucleic acid expression by administering to the subject an ACTR-1 ~~ATCR-1~~ modulator which is capable of modulating ACTR-1 ~~ATCR-1~~ protein activity or ACTR-1 ~~ATCR-1~~ nucleic acid expression.

In a preferred embodiment, the ACTR-1 ~~ATCR-1~~ molecules of the present invention are useful in methods for identifying modulators or are useful themselves as compositions for the diagnosis and treatment of disease or disorder that arise from malfunction of the regulation of triacylglycerol (triglyceride) and phospholipid biosynthesis (*e.g.,* atherosclerosis) as the molecules this invention are closely related to (e.g., orthologs of) the murine and rodent mitochondrial glycerol-3-phosphate acyltransferase (mGPAT), these proteins sharing greater than 90 percent sequence homology. There are two major forms of GPAT in mammalian tissues, microsomal and mitochondrial (Bell, R. M., and Coleman, R. A. (1983) in *The Enzymes* (Boyer, P. D., ed) pp. 87-89, Academic Press, New York). In liver, 50% of GPAT activity is found in the mitochondrial fraction, while in most other tissues microsomal GPAT activity is about 10 times that of the mitochondrial fraction (Schlossman, D. M., and Bell, R. M. (1976) *J. Biol. Chem.* 251, 5738-5744). GPAT, in general, has been shown to play a pivotal role in the regulation of triacylglycerol and phospholipid biosynthesis (Bell, R. M., and Coleman, R. A. *supra*). Triacylglycerol concentration is further involved in cardiovascular disease, including, but not limited to atherosclerosis. For example, increase in triacylglycerol level is a major risk factor for the development of atherosclerotic heart disease (Coleman RA *et al.* (2000) *Annu Rev Nutr* 20:77-103) and is also implicated in high blood pressure (Orchard TJ (2001) *Diabetes Care* 24:1053-9).

At page 81, line 22 through page 82, line 2, please replace the paragraphs with the following:

Homology searching using the amino acid and/or nucleotide sequence of human ACTR-1 ~~ATCR-1~~ revealed that the protein was significantly homologous (92%) to murine mitochondrial GPAT indicating that clone 56919 represents the human mitochondrial GPAT gene. Mitochondrial GPAT (mGPAT)

catalyzes the initial step in the biosynthesis of triglycerides. Triglycerides have been identified as independent risk factor for the development of atherosclerosis. Inhibitors of rodent mGPAT (endogenous and small molecules) have been described in the literature to exhibit triglyceride-lowering effects *in vivo*. Thus, human mGPAT is predicted to play a pivotal role in the regulation of triglyceride biosynthesis/metabolism in humans. Moreover, inhibition of human mitochondrial GPAT is predicted to result in decreased levels of serum triglyceride, which in turn will be beneficial in the treatment of atherosclerosis.

The amino acid sequence of human ACTR-1 was analyzed using the program PSORT (~~http://www.psort.nibb.ac.jp~~ www.psort.nibb.ac.jp) to predict the localization of the proteins within the cell. This program assesses the presence of different targeting and localization amino acid sequences within the query sequence. The results of the analyses show that human ACTR-1 may be localized to the nucleus, to the mitochondria, or to the cytoplasm. Based on homology to mouse and rat GPATS, human ACTR-1 ~~ATCR-1~~ is believed to be mitochondrial.

At page 86, lines 4-11, please replace the text with the following:

As indicated in Figures 7 and 8, strong expression of ACTR-1 was detected in the normal liver, adipose, heart and brain tissues. Moreover, as indicated in Figure 9, strong expression of the ACTR-1 ~~ATCR-1~~ was detected across a broad panel of human liver tissue samples.

EXAMPLE 5: UPREGULATION OF ACTR-1 ~~ATCR-1~~ IN AN IN VIVO MARMOSET CHOLESTYRAMINE MODEL.

At page 93, in the Title of the Abstract, please replace the text with the following:

ACTR-1 ~~ATCR-1~~, A NOVEL HUMAN ACYLTRANSFERASE AND USES THEREOF